

DETAILED ACTION

Applicants response filed 11/13/2008 is acknowledged.

Interview: In an interview with Susan A. Wolffe on 02/20/2009, it was agreed to recast Restriction/Requirement as follows:

Election/Restrictions

Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group 1, claim(s) 1, 5, 6, 10-33, 38-40, drawn to pyrazolopyrimidine compounds.

Group 2, claim(s) 34, 37, drawn to method of treating diseases using compounds of Group 1.

The inventions listed as Groups 1-2 do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: the common technical feature linking the groups is the pyrazolopyrimidine ring system. This moiety is not a contribution over the prior art as this is shown in US 4093617.

During a telephone conversation with Susan A. Wolffe on 02/20/2009 a provisional election was made with traverse to prosecute the invention of Group 1,

claims 1, 5, 6, 10-33, 38-40. Affirmation of this election must be made by applicant in replying to this Office action. Claims 34-37 withdrawn from further consideration by the examiner, 37 CFR 1.142 (b), as being drawn to a non-elected inventions.

Election/Restrictions: Traversal is on the grounds that there would not be undue burden to search the inventions together. For reasons given above the inventions listed as Groups 1-2 do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

It is suggested that applicant provide a clean copy of the claims, change the claim identifiers appropriately and correct typographical errors, claim dependency etc. See new rejections under 35 USC § 112 second paragraph.

Response to Applicants Remarks filed 11/10/2008:

Claim Rejections - 35 USC § 112

Applicants amendments to claims and persuasive arguments overcome the previously presented rejections under 35 USC § 112 first and second paragraphs.

Claim Rejections - 35 USC § 103

Applicants amendments to claims and persuasive arguments overcome the previously presented rejections under 35 USC § 103.

New Rejections:

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 5, 6, 10-33, 38-40, rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims are drawn to N-oxide, but it is unclear which nitrogen(s) of the formula has the N-O linkage.

Claims are drawn to hydrate and solvates without explicitly defining the chemical composition of solvates and hydrates protection is sought for. Solvates and hydrates are defined in the art with chemical formulae such as C8H6N2.HCl. 1.25 H2O.

Deletion of the terms N-oxide, hydrate or solvate would overcome this rejection.

Objection: Applicant is encouraged to correct typographical errors. For example, the need for the definition of Alk; the margins on second page of claim 1 in the definition of R1 etc.; R1 definitions in claim 30 etc.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 5, 6, 10-33, 38-40, rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making salts of compounds of the formula (I) does not reasonably provide enablement for making hydrates or solvates of N-oxides of the compounds of formula (I). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The determination that "undue experimentation" would have been needed to make and use the claimed invention is not a single, simple factual determination. Rather, it is a conclusion reached by weighing all the relevant factual considerations.

Enablement is considered in view of the Wands factors (MPEP 2164.01 (a)). These include: (1) breadth of the claims; (2) nature of the invention; (3) state of the prior art; (4) amount of direction provided by the inventor; (5) the level of predictability

in the art; (6) the existence of working examples; (7) quantity of experimentation needed to make or use the invention based on the content of the disclosure; and (8) relative skill in the art.

The specification does not reasonably provide enablement for making solvates or hydrates of the claimed compounds. The specification does not enable any person skilled in the art of synthetic organic chemistry to make the invention commensurate in scope with these claims. The factors to be considered in making an enablement rejection have been summarized above. In the present case the important factors leading to a conclusion of undue experimentation are the absence of any working example of a formed solvate, the lack of predictability in the art, and the broad scope of the claims. c) There is no working example of any solvate or solvate formed. The claims are drawn to solvates, yet the numerous examples presented all failed to produce a solvate. These cannot be simply willed into existence. As was stated in *Morton International Inc. v. Cardinal Chemical Co.*, 28 USPQ2d 1190 "The specification purports to teach, with over fifty examples, the preparation of the claimed compounds with the required connectivity. However ... there is no evidence that such compounds exist.., the examples of the '881 patent do not produce the postulated compounds.., there is ... no evidence that such compounds even exist." The same circumstance appears to be true here. There is no evidence that solvates of these compounds actually exist; if they did, they would have formed. Hence, applicants must show that solvates can be made, or limit the claims accordingly. g) The state of the art is that is not predictable whether solvates will form or what their

composition will be. In the language of the physical chemist, a solvate of organic molecule is an interstitial solid solution. This phrase is defined in the second paragraph on page 358 of West (Solid State Chemistry). The solvent molecule is a species introduced into the crystal and no part of the organic host molecule is left out or replaced. In the first paragraph on page 365, West (Solid-State Chemistry) says, "it is not usually possible to predict whether solid solutions will form, or if they do form what is their compositional extent". Thus, in the absence of experimentation one cannot predict if a particular solvent will solvate any particular crystal. One cannot predict the stoichiometry of the formed solvate, i.e. if one, two, or a half a molecule of solvent added per molecule of host. In the same paragraph on page 365 West (Solid State Chemistry) explains that it impossible to make meta-stable non-equilibrium solvates, further clouding what Applicants mean by the word solvate. Compared with polymorphs, there is an additional degree of freedom to solvates, which means a different solvent or even the moisture of the air that might change the stable region of the solvate. h) The breadth of the claims includes all of the hundreds of thousands of compounds of formula (I) as well as the presently unknown list of solvents embraced by the term "solvate".

Likewise, the specification is not enabling for making N-oxides of the compounds of formula (I). Compounds of the instant formula (I) contain at least four similar nitrogens, similar in terms of electron density which in turn determines the proclivity of the nitrogens to be oxidized (to make the corresponding N-oxide). It is not seen where in the specification, direction, guidance or working example is present for making any N-

oxide, let alone, reogioselective/regiospecific oxidation. These cannot be simply willed into existence. The specification is also silent with regards to prior art teachings for protocols for reogioselective/regiospecific oxidation reaction. As such, it would require undue amount of experiment to arrive at chemistry schemes to make N-oxides of compounds of instant formula (I).

Further, biological properties of N-oxides (relevant to 'use aspect' of the enablement requirement) are anticipated to be different from the corresponding basic amino compounds, unless there is (in vivo) biological reduction of the N-oxides to the basic amines. There is no enabling disclosure with regards to this phenomenon.

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ 2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here.

Deletion of the terms N-oxide, hydrate or solvate would overcome this rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact

terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 5, 6, 10-33, 38-40, rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims are drawn to N-oxides or hydrates or solvates compounds of formula (I). The working examples in the specification include physical characterization (such as NMR spectra) of a large number of compounds of the instant formula. None of the Examples have any data to show that any of the disclosed compounds formed N-oxides or hydrates or solvates (which would have been apparent in the NMR spectra).

Deletion of the terms N-oxide, hydrate or solvate would overcome this rejection.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

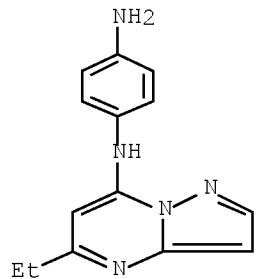
A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 5, 6, 10-33, 38-40 rejected under 35 U.S.C. 102(b) as being anticipated by prior art.

Ruehter et. al. US 5602136 5688949 7067661 20060205743

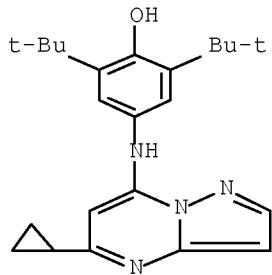
Claim 1,



R1 is B with a, b being 0, d being 1 and Alk4 being C-alkylene, B is H, R is H, p and s are 0, r is 1, x is O, Z is H

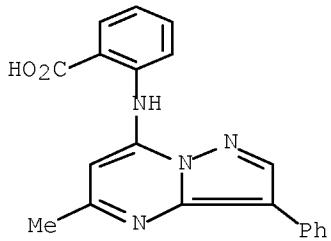
Inoue et al US 5688949 teach

Claim 1, 10,



R1 is B with a, b, d being 0, B is monocyclic, R is H, p and s are 0, r is 1, x is O, Z is H

Claim1, 5, 10,



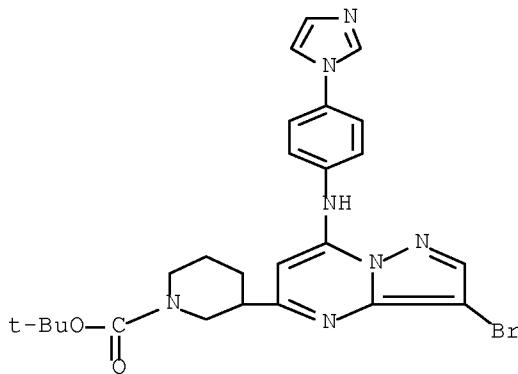
● Na

R1 is B with a, b, d being 0, B is phenyl, R is C1alkyl, p and s are 0, r is 1, X is – C(=O)O-, Z is H

Likewise,

Guzi et al. US 7067661, priority date 09-02-2002 teach

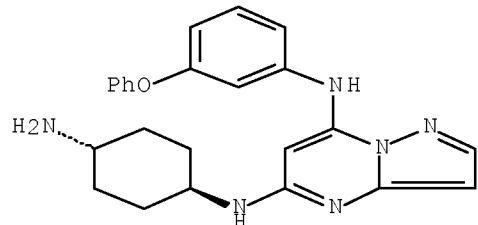
Claim 1, 11, 17, 18, 31,32



R1 is B with a, b, d being 0, B is optionally substituted heterocyclic, R is halo, Z is heterocyclic ring.

Kataoka et al. US 20060205743 priority GB-0305559.7 03-11-2003. teach

Claim 13, 23-26, 27, 28, 33, 30



X is O, r –s 1, Z is carbocyclic, R is hydrogen, B is H, Y is NRA RA being H, a, d is 0.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1, 5, 6, 10-33, 38-40 rejected under 35 U.S.C.103(a) as being unpatentable over Ruehter et. al. US 5602136.

Ruehter et. al. teach Pyrazolo[1,5-a]pyrimidin-7-amine derivatives as angiotensin antagonists. The compounds exemplified include compounds encompassed by the formula of the instant base claim 1 (see rejection under 102(b)).

Ruehter et al. do not teach all conceivable compounds of the instant formula. Ruehter et al. is also silent with regards to all conceivable biological properties of compounds of the instant formula. However compounds and its properties are inseparable and as such, it would be reasonable to expect, inherent, kinase activity for Ruehter compounds or its structural analogs. Hence one of skilled in the art would be motivated to make additional analogs of Ruehter et al. and explore their additional pharmaceutical use. The instantly claimed compounds would have been suggested and thus obvious to one of skill in the art.

Claims 1, 5, 6, 10-33, 38-40 rejected under 35 U.S.C. 103(a) as being unpatentable over Inoue et al US 5688949

Inoue et al. teach Pyrazolo[1,5-a]pyrimidin-7-amine derivatives as angiotensin antagonists. The compounds exemplified include compounds encompassed by the formula of the instant base claim 1 (see rejection under 102(b)).

Inoue et al. do not teach all conceivable compounds of the instant formulae 7-amino- Pyrazolo[1,5-a]pyrimidin-7-amine derivatives; Inoue et al. is also silent with regards to all conceivable biological properties of Pyrazolo[1,5-a]pyrimidin-7-amine

derivatives. However compounds and its properties are inseparable and as such, it would be reasonable to expect, inherent, kinase activity for Inoue compounds or its structural analogs. Hence one of skilled in the art would be motivated to make additional analogs of Inoue et al. and explore their additional pharmaceutical use. The instantly claimed compounds would have been suggested and thus obvious to one of skill in the art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to NIZAL S. CHANDRAKUMAR whose telephone number is (571)272-6202. The examiner can normally be reached on 8.30 AM - 4.30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on 571 0272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Application/Control Number: 10/551,177
Art Unit: 1625

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